REMARKS/ARGUMENTS

Reconsideration and continued examination of the above-identified application are respectfully requested.

By way of this amendment, claims 1-6, 9-16, 19, and 20 are pending. Claims 1-6, 9, 10, 12-16, 19, and 20 have been amended to replace the term "medicament" with the term "method." Claims 7, 8, 17, and 18 have been canceled. All of the claims now relate to a method for treating adhesion formation. It is noted that claim 11, which was examined, related specifically to a method for treating adhesion formation and, therefore, the conversion of the remaining claims to method claims would still be considered part of the examined application and would raise no reason to issue a restriction requirement. Accordingly, no questions of new matter should arise and entry of this amendment is respectfully requested.

Rejection of claims 1-6, 8, 10, and 19-20 under 35 U.S.C. §102(b) -- Powers et al.

Beginning at page 2 of the Office Action and continuing to page 3, the Examiner reasserts that claims 1-6, 8, 10, and 19-20 are rejected under 35 U.S.C. § 102 (b) as being anticipated by Powers et al. (U.S. Patent No. 5,543,396). The Examiner alleges that Powers et al. teaches a pharmaceutical composition comprising protease inhibitors such as Suc-Val-Pro-Phe^{P}(Oph)$_2$, which the Examiner states is described as the "best inhibitor for chymotrypsin and chymotrypsin-like enzymes." The Examiner states that since the present claims are product claims, the applicants' arguments presented in the response filed April 10, 2007 distinguishing between the intended use disclosed in Powers et al. and the intended use of the presently claimed invention were not deemed persuasive. The rejection in its entirety is respectfully traversed.

As stated above, claims 1-6, 8, 10, and 19-20, as currently amended, are now directed to

methods for treating adhesion formation of the tissue surface within a vertebrate subject. As explained in the applicants' previous Amendment filed April 10, 2007, Powers et al. does not teach or suggest the pharmaceutical activities of reducing or treating adhesion formation. As such, the applicants respectfully submit that this rejection is rendered moot.

Accordingly, this rejection should be withdrawn.

Rejection of claims 1-8, 10, 11, and 19-20 under 35 U.S.C. §102(b) -- Okamoto

At page 3 of the Office Action, the Examiner asserts that claims 1-8, 10, 11, and 19-20 are rejected under 35 U.S.C. § 102 (b) as being anticipated by Okamoto et al. (EUR. J. PHARMACOL., January 2002, 435(2-3): 265-7). The Examiner states that Okamoto et al. teaches a pharmaceutical composition comprising protease inhibitors such as Suc-Val-Pro-Phe^{P}(Oph)$_2$ for treating tissue adhesion. This rejection in its entirety is respectfully traversed.

The claims, as currently amended, are directed to methods for treating adhesion formation of the tissue surface within a vertebrate subject, comprising administering to the subject an effective amount of at least one protease inhibitor intravenously, orally, or percutaneously. Okamoto et al. discusses only injecting a chymase inhibitor into the abdomen of hamsters after resection of the right uterine body. Okamoto et al. does not discuss other routes of administration and the Examiner does not indicate that other routes of administration are mentioned in Okamoto et al. As discussed in the specification, the present inventors have found that tissue adhesion can be effectively treated by administering at least one protease inhibitor intravenously, orally, or percutaneously. The applicants respectfully submit that Okamoto et al. does not teach administration of at least one protease inhibitor intravenously, orally, or percutaneously. The applicants note that the Examiner is relying only on the abstract of Okamoto et al. However, in

the rejection, while the Examiner indicates that the rejection is based on the abstract only of Okamoto et al., the Examiner then asserts that Okamoto et al. teaches a composition and puts the following: "(entire document)." However, the Examiner has not provided a copy of the entire document and, therefore, the Examiner's reference to the "entire document" is confusing and appears to be incorrect. Further, the Board of Patent Appeals and Interferences, as well as the MPEP, have highly encouraged, if not required, the reliance on the full document as opposed to only an abstract since an abstract can be misleading. The Examiner is respectfully requested to provide a full document in English should the Examiner maintain this rejection and provide such a full document by way of a non-final Office Action. Accordingly, the applicants respectfully request withdrawal of this rejection.

Rejection of claims 1-20 under 35 U.S.C. §102(e) -- Miyazaki

Beginning at page 3 of the Office Action and continuing to page 4, the Examiner states that claims 1-20 are rejected under 35 U.S.C. § 102 (e) as being anticipated by Miyazaki (U.S. Patent Application Publication No. 2004/0018984). The Examiner states that Miyazaki teaches a pharmaceutical composition in any form comprising protease inhibitors such as Suc-Val-Pro-$Phe^{P}(Oph)_2$ for treating tissue adhesion. The Examiner states that because the reference has only one common inventor with the instant application (Miyazaki), it is an appropriate reference under 35 U.S.C. § 102 (e). This rejection in its entirety is respectfully traversed.

The applicants respectfully point out that Miyazaki (U.S. Patent Application Publication No. 2004/0018984) recites administering a drug to a site at which it is desired to prevent or reduce adhesion formation (e.g., abdominal, thoracic, ophthalmic, cardiac, or gynecologic tissue). Miyazaki (U.S. Patent Application Publication No. 2004/0018984) does not teach or suggest

methods for treating adhesion formation of the tissue surface within a vertebrate subject, comprising administering to the subject an effective amount of at least one protease inhibitor intravenously, orally, or percutaneously, as recited in the presently amended claims. Accordingly, the applicants respectfully submit that Miyazaki (U.S. Patent Application Publication No. 2004/0018984) is not an anticipating reference.

It is understood that the inventors of the present application are the authors of the subject matter disclosed but not claimed in Miyazaki (U.S. Patent Application Publication No. 2004/0018984). Thus, Miyazaki (U.S. Patent Application Publication No. 2004/0018984) does not constitute an application "by another." If the Examiner maintains this rejection, the applicants can submit a declaration under 37 C.F.R. § 1.132.

Accordingly, this rejection should be withdrawn.

Rejection of claims 1-8, 10, 11, and 19-20 under 35 U.S.C. §102(a) -- Akahoshi

At page 4 of the Office Action, the Examiner asserts that claims 1-8, 10, 11, and 19-20 are rejected under 35 U.S.C. § 102 (a) as being anticipated by Akahoshi (DRUGS OF THE FUTURE (2002), 27(8), 765-770). The Examiner states that Akahoshi teaches a pharmaceutical composition comprising protease inhibitors such as Suc-Val-Pro-Phe^{P}(Oph)$_2$ for treating tissue adhesion. This rejection is respectfully traversed.

With respect to the Akahoshi reference (as for Okamoto et al.), it is improper for the Examiner to only rely on the abstract for the rejection, without providing a full copy of the underlying document. In particular, M.P.E.P. §706.02 states that "Citation of and reliance upon an abstract without citation of and reliance upon the underlying scientific document is generally inappropriate where both the abstract and the underlying document are prior art. See *Ex parte*

Jones, 62 U.S.P.Q.2d 1206, 1208 (Bd. Pat. App. & Inter. 2001) (unpublished). Also, the Examiner refers to the "entire document" and no "entire document" has been provided.

Also, the claims, as currently amended, are directed to methods for treating adhesion formation of the tissue surface within a vertebrate subject, comprising administering to the subject an effective amount of at least one protease inhibitor intravenously, orally, or percutaneously. The abstract of Akahoshi does not teach or suggest administering a protease inhibitor intravenously, orally, or percutaneously. The Examiner also does not indicate where Akahoshi teaches administration of at least one protease inhibitor intravenously, orally, or percutaneously. Accordingly, the applicants also respectfully request withdrawal of this rejection.

Rejection of claims 1-20 under 35 U.S.C. §103(a) – Okamoto or Akahoshi in view of Scharpe et al. and Powers et al.

At page 5 of the Office Action, the Examiner asserts that claims 1-20 are rejected under 35 U.S.C. § 103 (a) as being unpatentable over Okamoto or Akahoshi in view of Scharpe et al (U.S. Patent Application Publication No. 2002/0061839) and Powers et al. The Examiner acknowledges that Powers et al. does not expressly teach the use of protease inhibitors such as Suc-Val-Pro-$Phe^{P}(Oph)_2$ to reduce tissue adhesion or all the various forms of administration. The Examiner states, however, that it would have been obvious to put protease inhibitors in any formulation in the composition of either Okamoto et al. or Akahoshi because the Examiner alleges that Scharpe et al. teaches that serine protease inhibitors may be put in compositions with liposomes, depending on the desired result and administration route. This rejection in its entirety is respectfully traversed.

The claimed invention relates to a method for treating tissue adhesion by administering at least one protease inhibitor intravenously, orally, or percutaneously. As discussed in the present

specification, the present inventors have found that tissue adhesion which occurs following surgical operations and tissue adhesion which is caused by an inflammation in the body can both be effectively treated by administering at least one protease inhibitor intravenously, orally, or percutaneously. While the Okamoto et al. and Akahoshi references may vaguely refer to tissue adhesion, neither reference teaches or suggests treating tissue adhesion by administering a protease inhibitor to a subject intravenously, orally, or percutaneously.

Since Scharpe et al. and Powers et al. do not at all relate to the treatment of adhesion formation, one skilled in the art simply will not look to these references for any guidance in determining an administrating route for purposes of adhesion formation. It is not reasonable to suggest that in determining an effective route for administering the drugs mentioned in Okamoto et al. and Akahoshi, one of ordinary skill in the art would rely upon the teachings of Scharpe et al. and Powers et al. As neither Scharpe et al. nor Powers et al. relate to treatments for tissue adhesion, one of ordinary skill in the art would not be motivated to rely upon Scharpe et al. or Powers et al. to determine an effective administration route for treating tissue adhesion. While Powers et al. and Scharpe et al. make reference to tissue remodeling, tissue remodeling is not equivalent or a genus of tissue adhesion formation. In addition, neither Powers et al. nor Scharpe et al. teach or suggest that tissue remodeling encompasses tissue adhesion formation. One skilled in the art also would readily recognize the difference between tissue remodeling and tissue adhesion formation. Tissue remodeling generally involves the remodeling or rebuilding of damaged tissue, which, many times, is carried out through changing the formation of the tissue itself. Adhesion formation is quite different from tissue remodeling. As described at the bottom of page 1 and top of page 2 of the present application, adhesion formation and adhesion-free re-epithelialization are alternative pathways, both of which begin with coagulation and which can result in the build-up of

fibrin gel matrix, and if this fibrin deposition is in excess or not removed, the gel matrix serves as a progenitor to adhesions by forming a band or bridge when two tissue surfaces coated with fibrin matrix are apposed. Accordingly, the applicants respectfully submit that use of protease inhibitors for reducing adhesion formation between tissue surfaces differs from use of protease inhibitors for anti-coagulant, anti-inflammatory, and tissue remodeling purposes.

Even if one could somehow rely upon Scharpe et al. or Powers et al., it is not clear how one would arrive at the presently claimed invention. One of ordinary skill in the art could not determine without undue experimentation which route or combinations of administration routes in Scharpe et al. and Powers et al. would be effective for treating tissue adhesion. The applicants note that both Scharpe et al. and Powers et al. suggest numerous routes of administration. For example, the applicants note that Powers et al. indicates that for treatment of blood coagulation-related diseases, tumor invasion, inflammation, organ transplant rejection, AIDS, or for controlling the immune system, compounds can be administered orally, topically, by subcutaneous injection, intravenously, intramuscularly, by intrasternal injection, or by infusion techniques (col. 16, lines 23-29). Similarly, Scharpe et al. lists many routes of administration, including, oral, rectal, topical, bucal, and nasal (para. 0125). The Examiner does not explain how one of ordinary skill in the art would arrive at the specific routes of administration recited in the present claims from the extensive list of possible administration routes provided in Scharpe et al. and Powers et al. The applicants respectfully submit, therefore, that the references cited by the Examiner do not render obvious the presently claimed invention. Accordingly, this rejection should be withdrawn.

Rejection of claims 1-20 under 35 U.S.C. §103(a) -- Powers et al. in view of Scharpe et al. and Okamoto or Akahoshi

At page 6 of the Office Action, the Examiner states that claims 1-20 are rejected under 35 U.S.C. § 103 (a) as being unpatentable over Powers et al. in view of Scharpe et al. and Okamoto or Akahoshi. The Examiner states that it would have been obvious to use any protease inhibitor as one of the methods relevant to inhibiting the actions of the serine protease chymotrypsin because Scharpe et al. teaches the use of protease inhibitors to inhibit chymotrypsin. The Examiner suggests that chymotrypsin is known to be used in the pathway of tissue remodeling and tissue adhesion. The Examiner states that it would have been obvious to put protease inhibitors in any formulation in the composition of either Okamoto or Akahoshi because, the Examiner alleges that Scharpe et al. teaches that serine protease inhibitors may be put in composition with liposomes, depending on the desired result and administration route. This rejection in its entirety is respectfully traversed.

As discussed previously, neither Powers et al. nor Scharpe et al. teach or suggest a treatment for tissue adhesion. The Examiner suggests that it would have been obvious to one of ordinary skill in the art to combine the teachings of Powers et al. with Scharpe et al., Okamoto et al., and Akahoshi to arrive at the presently claimed methods for treating tissue adhesion. The primary purpose of Powers et al., however, is to use certain derivatives as anti-coagulants, anti-inflammatory agents, and anti-tumor agents. As Powers et al. fails to provide any guidance or motivation for treating tissue adhesion, one of ordinary skill in the art would not be motivated to combine the teachings of Powers et al. with Okamoto et al. or Akahoshi. Even if the teachings of Powers et al. and the secondary references cited by the Examiner could somehow be properly combined, one would not arrive at the presently claimed invention. Neither Okamoto et al. nor Akahoshi teach or suggest administering a protease inhibitor to a subject intravenously, orally, or percutaneously. While both Scharpe et al. and Powers et al. do suggest numerous routes of administration, it is

unclear, as discussed above, how one of ordinary skill in the art would arrive at the specific routes of administration recited in the present claims from the extensive list of possible administration routes provided in Scharpe et al. and Powers et al. As such, the applicants respectfully submit that by combining the teachings of Powers et al. with the secondary references cited by the Examiner, one of ordinary skill in the art would not arrive at the presently claimed invention.

Accordingly, this rejection should be withdrawn.

Rejection of claim 1-20 -- Non-statutory obviousness-type double patenting

At page 9 of the Office Action, the Examiner states that claims 1-20 are provisionally rejected on the ground of non-statutory obviousness-type double patenting as being unpatentable over claims 1-7, 10-12, 30, and 33 of co-pending Application No. 10/602,035. Although the same routes of administration are not claimed, the Examiner states that routes of administering the protease inhibitors would have been readily apparent to one of ordinary skill in the art. This rejection is respectfully traversed.

Since this is a provisional rejection, once the remaining rejections described above have been overcome, this provisional rejection should be withdrawn and, if necessary, applied in co-pending U.S. Patent Application No. 10/602,035. The Examiner, at page 9 of the Office Action, states that the "analysis turns on the claims, yet the specification remains used as guide where 'comprising' language in base claims leaves open the routes of administration . . ." The applicants respectfully request the Examiner to identify the legal foundation and MPEP cite that supports this statement by the Examiner. The applicants are unaware of any legal cite or MPEP section that would support this particular position taken by Examiner. Accordingly, this provisional rejection

should be withdrawn once it is the only remaining rejection in the present application.

Accordingly, this rejection should be withdrawn.

Rejection of claims 6-8 under 35 U.S.C. §112

At page 10 of the Office Action, the Examiner indicates that the previous rejection of claims 6-8 under 35 U.S.C. § 112, second paragraph, is rendered moot. It is the Examiner's understanding that the compounds recited in claims 6-8 are all the same compound, in L form. The Examiner states that all peptides are generally understood to be in the L form unless the alternative D form is indicated. This rejection is rejection is respectfully traversed.

The applicants cannot fully agree with the Examiner's statements, but since claims 7 and 8 are canceled, it will no longer be an issue. Accordingly, this rejection should be withdrawn.

CONCLUSION

In view of the foregoing remarks, the applicant respectfully requests the reconsideration of this application and the timely allowance of the pending claims.

If there are any fees due in connection with the filing of this response, please charge the fees to our Deposit Account No. 50-0925. If a fee is required for an extension of time under 37 C.F.R. § 1.136 not accounted for above, such extension is requested and should also be charged to said Deposit Account.

Respectfully submitted,

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